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COMMENTS

Claims 11, 13, 18-22, and 83 are pending and under examination in the present case. Claims 11 and 13 have been amended and claim 83 has been cancelled herein without prejudice or disclaimer. Claims 89-91 have been added. Upon entry of this amendment, claims 11, 13, 18-22, and 89-91 will be pending and under consideration. Entry of the amendments and reconsideration of the application in view of the amendments herein is respectfully requested.

No new matter is added with the amendments to the specification and claims. Various paragraphs of the specification were amended to eliminate hypertext links. Claim 11 has been amended to incorporate elements of claim 1 as filed, from which it previously depended. Furthermore, claim 11 is amended herein to specify hybridization conditions, as supported, for example, by page 16, lines 5-6. The amendments to claim 13 deletes elements. Newly added claim 89 is supported, for example, by Page 52, lines 4-8, and claim 4 as filed. Newly added claim 90 is supported, for example, by page 16, lines 5-6. Newly added claim 91 is supported, for example, by page 10, lines 5-8.

Specification Objections

The specification stands objected to as allegedly including browser-executable code. The specification as amended does not include browser-executable code. Accordingly, Applicants respectfully request that the objection to the specification be withdrawn.

Claim Objections

Claims 11 and 83 stand objected to for depending from non-elected claims. Claim 83 is cancelled herein. Accordingly the rejection is moot with respect to claim 83. Claims 11 as amended herein is an independent claim. Therefore, the objection is overcome with respect to claim 11. Accordingly, Applicants respectfully request withdrawal of the objection.

Claim Rejection Under 35 U.S.C. § 112, First Paragraph-Enablement

Claims 11, 13, 18-22, and 83 stand rejected under 35 U.S.C. § 112, first paragraph because the specification allegedly does not enable all polynucleotides encompassed by these claims. The Office Action acknowledges that the Applicants are in possession of the polynucleotide of SEQ ID NO:3 and polynucleotides encoding GTRAP4-48, SEQ ID NO:4, as well as full-length complements thereof. However, the Office Action alleges that the claims embrace an infinite number of polynucleotides encoding an infinite number of GTRAP polypeptides. The Office Action alleges that no working examples are provided to identify which amino acids are necessary to maintain the functions of the polypeptides encoded by the claimed polynucleotides. Furthermore, the Office Action alleges that the Applicants have provided little guidance, beyond presentation of primary sequence data, regarding which positions in the encoded protein are tolerant to change, and the nature and extent of the change tolerated.

The pending claims rejected under 35 U.S.C. § 112, first paragraph, all depend from claims 11 and 13. Claim 11 recites both structural and functional elements regarding the claimed polynucleotide. For example, claim 11 as amended recites that the claimed polynucleotide encodes a polypeptide that functions to modulate intracellular glutamate transport and to interact with a glutamate transporter protein. Furthermore, claim 11 as amended recites that structurally, the claimed polynucleotide hybridizes under conditions of 0.2x SSC, 0.1% SDS, at 42°C to a polynucleotide encoding a polypeptide having the amino acid sequence as set forth in SEQ ID NO:4. Therefore, the claim does not encompass an infinite number of polynucleotides, as alleged, but rather encompasses polynucleotides having recited functions and a defined structure. A skilled artisan can readily determine whether a polynucleotide falls within the claims by performing routine hybridization experimentation under the defined conditions and routine functional experiments using, for example, the methods taught in the specification.

Applicants respectfully assert that the specification provides adequate disclosure regarding regions of polypeptides encoded by the claimed polynucleotides that are important for the recited functions, to allow manipulations of the primary sequence using routine

experimentation, while retaining the functions recited in claim 11. For example, the specification discloses that GTRAP4-48, whose complete sequence is disclosed in SEQ ID NO:4, includes a PDZ domain, a regulatory G-protein domain, a pleckstrin homology region, and a proline-rich sequence (Pg. 52, lines 4-8; and claim 4 as filed). Furthermore, the specification discloses that these regions are believed to be involved in protein-protein interactions by interacting with the C-terminus of proteins, and are thought to be important in subcellular targeting of the interacting proteins (Id. citing (Katan *et al., FEBS Lett.* (1999) 452:36-40 (Exhibit A); LeVine, *Mol. Neurobiol.* (1999); 19:111-149 (Exhibit B)). Finally, the specification teaches that GTRAP4-48 co-localize with and binds to the glutamate transporter EAAT4 *in vivo* (Example 7), and that this interaction affects EAAT4 activity. Therefore, Applicants respectfully assert that the specification provides sufficient guidance regarding the relationship between various domains of polypeptides encoded by the claimed polynucleotides, and the recited functions of these encoded polypeptides. A skilled artisan can use routine techniques to identify claimed polynucleotides that encode a polypeptide with the recited functions (i.e., to modulate intracellular glutamate transport and to interact with a glutamate transport protein). Accordingly, Applicants respectfully assert that the present specification enables the polynucleotide of amended claim 11, and claims dependent therefrom.

It is also noteworthy that newly added claims 84, which depends from claim 11, is even more clearly enabled by the specification because it recites a polynucleotide that encodes a polypeptide that includes a PDZ domain, a regulatory G-protein domain, a pleckstrin homology region, and a proline-rich sequence. Furthermore, newly added claim 85 is directed at an isolated polynucleotide that hybridizes under conditions of 0.2x SSC, 0.1% SDS, at 42°C with a polynucleotide according to SEQ ID NO:3.

Regarding claim 13, the claimed polynucleotide has a structure (i.e., a nucleotide sequence) that can be determined based solely on information in the disclosure and routine computations, without further experimentation. Since the amino acid sequence of SEQ ID NO:4 is disclosed, polynucleotides that encode this polypeptide, including those where T can be U, and complements thereof, can be readily identified using the well-known genetic code and basic computations. One of

these sequences, SEQ ID NO:3, specifically recited in the claim, is disclosed in the application. Furthermore, from the disclosure of SEQ ID NO:4, polynucleotides of at least 15 nucleotides in length that encode at least a portion of this polypeptide can be readily determined. Accordingly, claim 13 encompasses polynucleotides of known sequence, not an infinite number of polynucleotides, as alleged in the Office Action.

Regarding the Office Action's allegation that claim 13 is not enabled because the 3-dimensional structures of the proteins encoded by all of the polynucleotides that fall within claim 13 are not known, Applicants respectfully assert that such information is not necessary to enable claim 13. This conclusion is based on the fact that polynucleotides of claim 13, and claims depending therefrom, are useful as probes, or for the synthesis of complementary probes, to detect polynucleotides that encode all or a portion of SEQ ID NO:4. Therefore, a skilled artisan can make and use polynucleotides according to claim 13, without knowing the precise structure of a polypeptide encoded by a claimed polynucleotide. In summary, Applicants respectfully assert that independent claims 11 and 13, as well as dependent claims 18-22, and 83, are enabled by the disclosure as filed. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 11, 13, 18-22 and 83 under 35 U.S.C. § 112, first Paragraph.

Claim Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 13 stands rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite in reciting a degenerate sequence of a complement, referring to element 13(e). Applicants traverse the rejection. Claim 13 as amended does not recite a degenerate of a complement. Therefore, the rejection has been overcome and Applicants respectfully request withdrawal of the rejection of claim 13 under 35 U.S.C. § 112, second paragraph.

If the Examiner believes that a telephonic or personal interview would be helpful to terminate any issues which may remain in the prosecution of the Application, the Examiner is requested to telephone Applicants' attorney at the telephone number set forth herein below.

The Commissioner is hereby authorized to charge any additional fees which may be required in the Application to Deposit Account No. 50-1135.

Respectfully submitted,

Dated: July 1, 2003

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1: FEBS Lett. 1999 Jun 4;452(1-2):36-40.

Modular PH and C2 domains in membrane attachment and other functions.

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The pleckstrin homology and C2 domains are modular protein structures involved in mediating intermolecular interactions. Although they represent distinct domains, there are several parallels regarding their function and type of interactions in which they participate. Both domains are stable structural entities that incorporate variable regions which, in different proteins, can be adapted to perform a specific function through binding to membrane phospholipids or specific protein ligands. A number of recent examples illustrate the function of some of these domains in regulated membrane attachment, with an important role in many cellular signalling pathways.

Publication Types:
- Review
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